DECLARATION OF JEAN-LOUIS JUNIEN UNDER 37 CFR § 1.132

I, Jean-Louis JUNIEN, do hereby declare as follows:

I am a pharmacologist and highly experienced in the field of cardiometabolics. I have been working in FOURNIER Laboratories as head of Research and Development.

I have been working on fibrates and especially on fenofibrate and I used to work with Zucker rats as an animal model for experimentation.

I have been advised by the European patent attorney for the Assignee of the above-identified patent application that the US Patent Office Examiner of the above-identified patent application has questioned whether and how the use of the combination as claimed yields unexpected and superior results for treating obesity and how this is non-obvious in view of the references cited by the Examiner.

I have contributed to several patents filed mostly in France, with regular extension to the United States.

I am familiar with the English language and with the Office Actions issued by the American Patent Office during US patent prosecution.

I understand the prosecution history of the above-referenced patent application and I am especially aware of the contents of the first and second Office Actions.

I have reviewed the content of the above-identified patent application, including the enclosed amended claims as well as the prior art documents cited in the present prosecution.

The patent application relates to a method for treating obesity comprising administering to a patient a formulation of metformin and a PPARα agonist. More specifically, the claims are directed to such a method wherein the PPARα agonist is fenofibrate, fenofibric acid or a pharmaceutically acceptable salt of fenofibric acid.

From my point of view, it is clear that Example 3 of the patent application and in particular the results in Table 3 demonstrate that the administration of fenofibrate and metformin significantly lowers the body weight gain in obese rats and that the difference is superior to the addition of the effects of these two compounds when administered alone.

As specified on page 13, line 24-25 of the application, statistical analyses were conducted on the obtained experimental results. These analyses were carried out by using Dunnett's test. This test is an appropriate statistical test to compare each of the different test groups with a control group.

As a professional pharmacologist, it is clear when reading the results in Table 3 that they demonstrate that the use of metformin and fenofibrate leads to a reduction of the body weight gain in obese rats .

In addition, I am personally convinced that same results would be obtained by using fenofibric acid or a pharmaceutically acceptable salt of fenofibric acid instead of fenofibrate

combined with metformin, as the *in vivo* active form of fenofibrate is in fact the free acid (fenofibric acid) that could derived from the fenofibrate (ester) or any pharmaceuticaly acceptable salt of fenofibric acid.

From a careful reading of the references cited by the Examiner and considering the foregoing statement, it is my opinion that a worker in the field of pharmacology would not be led to specifically combine metformin and fenofibrate (or fenofibric acid or a salt of fenofibric acid) in a formulation to treat obesity. In addition, one skilled in the art could absolutely not predict that such a particular combination would have a significant effect on body weight reduction as depicted in Table 3.

Some prior art references are related to activity (which is often putative) of active compounds other than metformin and fenofibrate (*i.e.* new azole derivates, cannabinoid CB1 receptor antagonists, etc). The significance or relevance to optionally combine these compounds with additional ingredients (among which metformin and/or fenofibrate are sometimes cited) is never disclosed. And in any case, the combined disclosures of these references never suggest associating metformin and fenofibrate only (with no further compounds) for the treatment of obesity. In addition, almost all these references are related to various diseases or disorders without being specifically related to obesity.

Other references are related to body weight or obesity and to administering fenofibrate or metformin but only separately. I believe that the teaching of these references cannot make the present invention obvious as a worker in this field would not have any reason to presume the experimentally obtained effect on body weight reduction exhibited by the combined use of metformin and fenofibrate.

It is my opinion that the content of the cited references certainly does not suggest the unexpected results as depicted in Table 3 of the above-mentioned patent application.

Therefore, the invention as claimed is not obvious in view of the prior art because of the unexpected effect of the combination of both fenofibrate and metformin on body weight gain diminution.

Based on the above-reported comments, it is my opinion that there is no reason to believe that the combination of metformin with a fibrate selected form the group consisting in fenofibrate, fenofibric acid and a pharmaceutically acceptable salt of fenofibric acid could have led to the obtained effect on the diminution of the body weight gain.

I hereby declare that all statements made herein of my own knowledge are true, and that all statements made on information and belief are believed to be true; and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

DATE: 12/10/08

Jean-Louis Junien

BY: Jean-Louis JUNIEN